Nutritional modulation of cardiac disease

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KEY POINTS

- Nutrition can be an important adjunct to medical therapy in dogs and cats with cardiac disease.
- Maintaining optimal weight by avoiding obesity and cachexia is key to optimal management of cardiac disease.
- Excesses of certain nutrients, such as sodium and potassium, must be avoided.
- Nutritional deficiencies either as the cause of cardiac disease or a consequence of its treatment can occur. Adequate protein, taurine, B vitamins and potassium levels should be maintained.
- Certain nutrients may provide additional benefits above and beyond their nutritional effects. Nutrients currently being investigated for their potential pharmacological roles include omega-3 polyunsaturated fatty acids, coenzyme Q10 and antioxidants.

Introduction

The goal of nutrition for dogs and cats once was just to provide adequate calories, protein, fat, vitamins and minerals. Over the years, researchers have discovered that nutrition can also play an important role in the management of diseases, including cardiac disease. Our knowledge of the specific nutrients and the exact nutrient levels required in cardiac disease has been refined over the years. In the 1960s, the only nutritional recommendations for dogs with congestive heart failure (CHF) were to feed a low sodium diet for all stages of heart disease, to feed a restricted protein diet and to provide supplemental B vitamins (1). Few changes to these recommendations were made in the 1970s (2). In the 1980s, the question as to how early to institute sodium restriction was first raised (3). Protein restriction and potassium and B vitamin supplementation were recommended, and syndrome of cardiac cachexia was first mentioned (3). It was also in the late 1980s that the discovery of the relationship between taurine deficiency and feline dilated cardiomyopathy (DCM) was published (4). Now, in the year 2000, we have the benefit of new and more potent cardiac medications and renewed interest in research on the nutritional modulation in cardiac disease. Recent research has shown that nutrition actually can modulate cardiac disease, either by slowing the progression, minimising the number of medications required, improving quality of life or, in rare cases, actually curing the disease. Although researchers are just beginning to explore these areas, there is great potential for nutrition as an important adjunct to medical therapy for patients with cardiac disease.

Cardiac disease comes in various types, severity differs between animals, and individual patient differences exist. Therefore, each animal must be treated as an individual when deciding when to institute nutrient restriction or whether to institute nutritional supplementation. Nonetheless, one goal is key in all animals with cardiac disease – maintaining optimal weight.

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Optimal weight maintenance

When clinicians think of nutrition for patients with cardiac disease, they typically think of either nutritional excesses (e.g. sodium) or deficiencies (e.g. taurine). In fact, the most common nutritional problem in cardiac disease is a deficiency or excess of a different nutrient: calories. A key goal for the optimal management of cardiac disease is to maintain optimal body weight since both obesity and weight loss can adversely affect health.

Obesity

Obesity, a body weight greater than 20% over ideal, occurs in approximately 30–40% of dogs and cats in the United States. Therefore, it is likely that some patients with cardiac disease will be obese (**Figure 1**). It is important to rule out concurrent endocrine disease in patients that are obese, but most animals develop obesity as the result of overeating. Little research has been performed on the effects of obesity in dogs and cats with cardiac disease. Nonetheless, it is likely to be deleterious since obesity has adverse

Figure 1 *A dog with chronic valvular disease complicated by severe obesity. Obesity in this case may exacerbate the disease and weight reduction may help.*

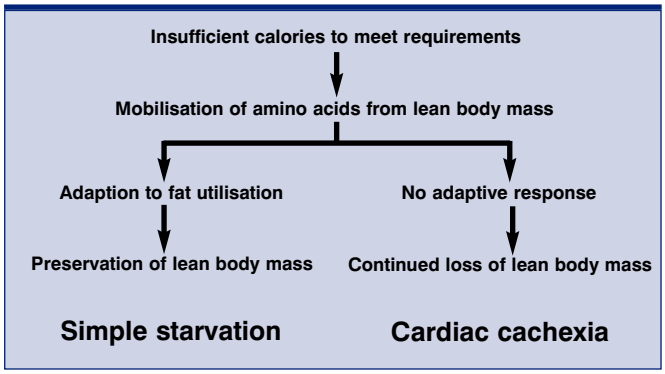


Figure 2 *There is a dramatic difference between simple starvation, which occurs in a healthy animal and cachexia, the weight loss seen in animals with cardiac disease. A healthy animal will primarily lose fat tissue, whereas cachexia is distinguished by a loss of lean body mass.*

effects on cardiac output, pulmonary function, neurohumoral activation, blood pressure and heart rate in people and in experimental animal models (5). Owners often find that severely obese dogs and cats with cardiac disease that successfully lose weight appear less dyspnoeic and more active.

Successful weight reduction is a difficult endeavour and often fails. Keys to success include:

- Giving the owner incentive (i.e. weight loss will help the dog feel better, weight loss will allow the cat to breathe more easily).
- Doing a careful dietary history to determine and control all sources of caloric intake, and follow-up support.
- Recommending a specific food and amount, rather than making the general recommendation to switch to a lower calorie food.
- Re-checking body weight after 2 weeks and if the animal is not losing weight, question the owner to find out other potential sources of calories.
- If the owner appears to be following your initial recommendations, reduce the amount of food further.
- Allowing low calorie, low salt treats such as vegetables often is helpful.

Cachexia

Cachexia is the wasting commonly seen in patients with CHF. In one study of dogs with DCM, over 50% of patients had some degree of cachexia (6). The weight loss that occurs in these patients is unlike that seen in a healthy dog or cat that loses weight (**Figure 2**). Any animal that is receiving insufficient calories to meet requirements, whether sick or healthy, will initially utilise amino acids generated from catabolism of lean body mass. This process occurs for several days until the healthy animal switches to fat utilisation to preserve lean body mass. Therefore, a healthy animal will primarily lose adipose tissue when he is not receiving adequate calories. Animals with an acute or chronic disease, including cardiac disease cannot make this adaptive change to fat utilisation and continue to catabolise lean body mass. Thus, the distinguishing feature of cachexia is a loss of lean body mass. This lean body mass loss has direct and deleterious effects on strength, immune function and survival (7). Cachexia has historically been viewed as an end-stage situation manifested by an emaciated dog or cat (**Figure 3**). Actually, cachexia is a process and can be very subtle initially (**Figure 4**). Learning to recognise this process at an early stage may provide better opportunities to manage it effectively.

The loss of lean body mass in cardiac cachexia is a multifactorial process caused by the adverse effects of anorexia, increased energy requirements and metabolic alterations (7). The anorexia may be secondary to the fatigue or dyspnoea often seen in patients with cardiac disease or may be due to medication toxicity or feeding an unpalatable diet (7). Caloric intake in one study of dogs with DCM was only 72–84% of expected energy requirements (6). Increased energy requirements may also play a role in cachexia since requirements of up to 30% above normal have been

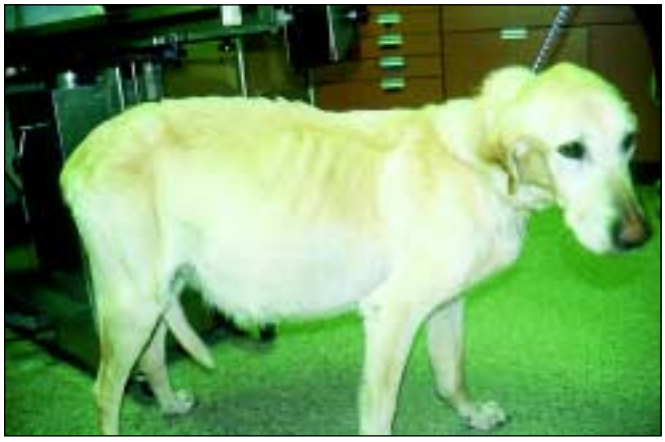


Figure 3 *Cardiac cachexia is often viewed as an end-stage situation like the dog shown here with severe dilated cardiomyopathy and congestive heart failure.*

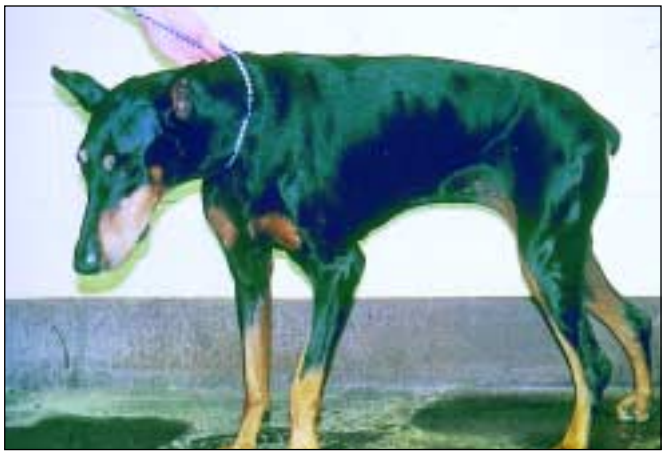


Figure 4 *Cardiac cachexia is actually a process during which lean body mass is gradually lost. Cachexia can be very subtle initially and may be manifested only by mild muscle loss over the epaxial and gluteal muscles.*

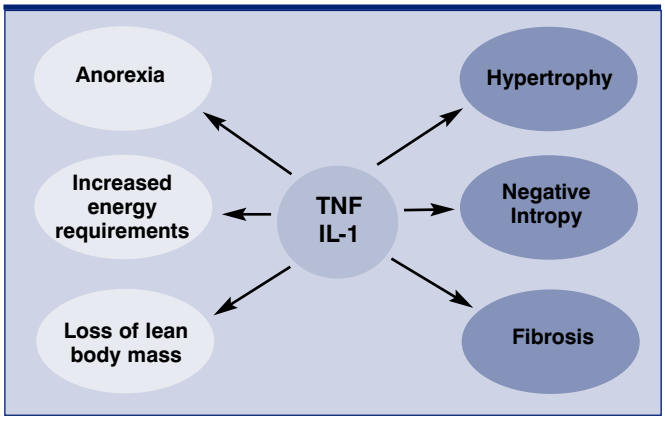


Figure 5 *Cardiovascular and nutritional effects of the inflammatory cytokines, tumour necrosis factor (TNF) and interleukin-1 (IL-1).*

documented in people with CHF (8). However, anorexia and increased energy requirements alone would not cause loss of lean body mass. While these factors play a role in the loss of lean body mass, a major factor is the elevation in the concentration of cytokines, tumour necrosis factor and interleukin-1 which occurs in CHF patients (7). These inflammatory mediators are known to directly cause anorexia, to increase energy requirements and to increase breakdown of lean body mass. In addition, both the above cytokines have negative inotropic effects and cause cardiac hypertrophy and fibrosis (**Figure 5**) (7). Cardiac cachexia is not usually seen in patients with cardiac disease until CHF has developed. It can be seen with any type of heart disease (i.e. chronic valvular disease, congenital cardiac diseases) but is most common in dogs with DCM, especially those with right-sided heart failure. Cachexia is less common in cats than in dogs. Loss of lean body mass is usually noted first in the epaxial, gluteal, scapular or temporal muscles, and can be subtle initially. The author scores all patients with cardiac disease for cachexia using a subjective score from 0 to 4 (**Figure 6**). Once clinicians are aware of cachexia and look for it in patients with cardiac disease, it can be detected at earlier stages.

At the current time, nutritional therapy of cardiac cachexia is limited to nutritional support for anorexia and nutritional modulation of cytokine production. Another important reason for managing anorexia is that the presence of anorexia is one of the most common factors that contributes to an owner's decision to euthanatise the pet (9). Keys to nutritional management of anorexia are shown in **Table 1**.

Modulation of cytokine production is another potential means of managing cardiac cachexia. One method of decreasing the production and effects of cytokines is with omega-3 polyunsaturated fatty acid (PUFA) supplementation (see below). Supplementation of fish oil, which is high in omega-3 PUFA, can decrease cytokine production in dogs with CHF and improve cachexia (6). In some, but not all dogs with CHF-induced anorexia, fish oil supplementation can improve food intake (6). In addition, reduction of cytokines has been correlated with survival in dogs with CHF (6).

Table 1

Keys to nutritional management of anorexia in patients with cardiac disease

1. Anorexia is sometimes an early sign of worsening heart failure and it is important to assess the patient for optimal medical control of heart failure
2. Assess the patient for digoxin toxicity or other medication intolerances
3. Change to a more palatable diet (e.g. canned to dry or dry to canned, a different brand, a balanced home-made diet)
4. Warm the food
5. Feed smaller, more frequent meals
6. Add flavour enhancers (for dogs, yoghurt, honey or cooked meat; for cats, cooked meat or fish or low-salt tuna juice)
7. Consider fish oil supplementation

Nutritional modulation of specific nutrients

At one time, nutritional deficiencies were a common cause of cardiac disease in people. Although these deficiencies are now uncommon, there still may be a number of examples in dogs and cats and deficiencies may develop secondary to the disease or its treatment. A new area of nutritional research is that of nutritional pharmacology, the idea that supplementation of certain nutrients may provide benefits above and beyond their nutritional effects. Described below are the nutrients most commonly proposed for use in dogs and cats with cardiac disease.

Protein and amino acids

Protein

As early as the 1960s, authors proposed restricted protein intake for dogs with congestive heart failure to prevent 'metabolic stress' on the kidneys and liver (1). There is no evidence that protein restriction is necessary for dogs and cats with CHF and, in fact, it probably is deleterious in these patients that are predisposed to loss of lean body mass. Unless severe renal dysfunction is present, high-quality protein should be fed to meet canine and feline maintenance requirements.

Taurine

Taurine is an amino acid that is found in high levels in the myocardium. Despite knowledge of the role of taurine deficiency in feline DCM, a small number of cats still develop DCM (4). Most current cases, however, are taurine-independent. Still, taurine deficiency should be suspected in all cases of feline DCM. A dietary history should be elicited from owners to determine whether the cat has been fed a poor quality, homemade, vegetarian or otherwise unbalanced diets. Plasma and whole blood taurine should be analysed, and treatment with taurine (125–250 mg PO BID) should begin concurrent with medical therapy. If the taurine concentration is found to be normal, taurine supplementation can be discontinued. Unlike cats, dogs are able to synthesise adequate amounts of taurine. Most dogs with DCM do not have taurine deficiency, but low taurine concentrations have been found in certain breeds of dogs with DCM, most notably the American Cocker Spaniel (10). One small study showed that cocker spaniels supplemented with taurine and carnitine had improvement in clinical parameters and echocardiographic measurements (11). Whether the response would be similar with either taurine or carnitine alone remains to be seen. In the author's experience, while some dogs of atypical breeds with DCM have low taurine concentrations, these dogs do not have a dramatic response to taurine or carnitine supplementation. Nonetheless, measurement of plasma and whole blood taurine concentrations is warranted in cocker spaniels and other atypical breeds with DCM. Supplementation with taurine (500 mg PO BID-TID) and carnitine (1 gm PO BID-TID) is recommended in dogs with documented taurine deficiency until additional research has been done.

Some of the benefits of taurine in dogs with low taurine concentrations may be due to its pharmacological effects. Taurine has some positive inotropic effects so has been used in animals with experimentally-induced heart failure and in unblinded human clinical trials, both demonstrating some benefits (12, 13). Although further research is required, taurine supplementation may have modest benefits in cardiac patients even without taurine deficiency.

Arginine

Unlike most other species, dogs and cats require dietary arginine, since adequate amounts cannot be synthesised endogenously. The cat has a particularly high requirement because of its evolution as a carnivore. In addition to its nutritional role, arginine is a precursor of nitric oxide, which inhibits platelet aggregation and adhesion, decreases vascular smooth muscle proliferation and maintains normal vasodilatory tone (14). A recent study showed that cats with arterial thromboembolism secondary to cardiomyopathy had lower circulating arginine concentrations than cats with either cardiomyopathy alone or healthy control cats (15). While these results may be merely the result of a consumptive process during thrombus formation or ischaemia, further studies are required to better understand the role of this amino acid in feline arterial thromboembolism.

Fat

In the past, the major role of fat in diets has been to provide calories and to increase the palatability of diets. It is now known that the type of fat ingested can significantly affect immunological, inflammatory and haemodynamic parameters. The omega-3 PUFA, eicosapentaenoeic acid (EPA) and docosahexaenoeic acid (DHA), are long-chain fatty acids in which the first double-bond is at the position of the 3rd carbon from the methyl end (vs. the omega-6 PUFA, linoleic, gamma-linolenic and arachidonic, in which the first double bond is at the 6th carbon). This difference conveys a different structure and characteristics to the fatty acid. Plasma membranes normally contain very low concentrations of omega-3 PUFA, but levels can be increased by a food or supplement enriched in omega-3 PUFA. Dogs with CHF have been shown to have plasma fatty acid abnormalities, including decreased concentrations of EPA and DHA compared to normal dogs (6). In one study of dogs with DCM and CHF, fish oil supplementation at a dose of 25 mg/kg EPA and 18 mg/kg DHA normalised these plasma fatty acid abnormalities (6). Another benefit of omega-3 PUFA supplementation is that breakdown products of the omega-3 PUFA (series 3 and 5 eicosanoids) are, in general, less potent inflammatory mediators than eicosanoids derived from omega-6 PUFA (series 2 and 4 eicosanoids). This decreases the production of cytokines and other inflammatory mediators which may reduce cachexia (6, 16). Fish oil will not benefit all dogs and cats with CHF, but the author currently recommends a dosage of 40 mg/kg EPA and 25 mg/kg DHA in dogs with anorexia or cachexia. The amount of EPA and DHA in individual fish oil supplements varies widely so it is important to know the exact amount in brand of supplement recommended. Capsules that contain approximately 180 mg EPA and 120 mg DHA can be purchased over the counter at most human pharmacies or health food stores. Higher dosages can be obtained from medical supply catalogues and are more feasible for large dogs. Fish oil should contain vitamin E as an antioxidant, but other nutrients should not be included to avoid toxicities.

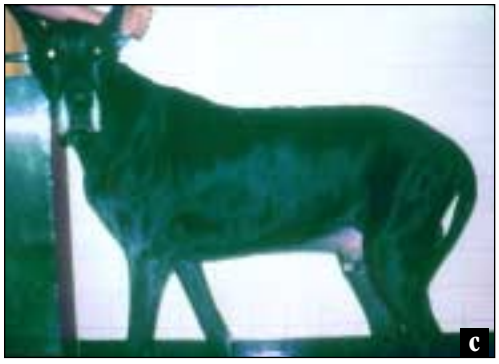
Minerals

Sodium

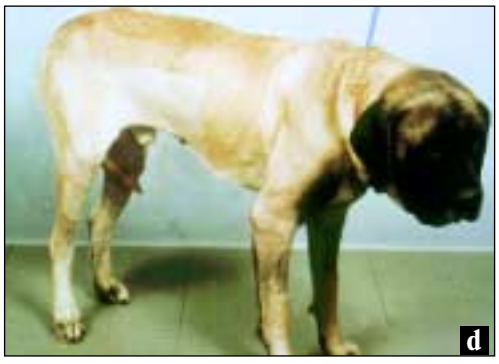
Although healthy animals can easily excrete excess dietary sodium in the urine, this response is blunted in animals with cardiac disease (17). Based on the pathogenesis, authors in the 1960s and 1970s recommended changing to a severely sodium restricted diet when a heart murmur was first detected, even before clinical signs were present. It is unnecessary to institute severe sodium restriction at this early stage. As heart disease progresses and CHF ensues, however, sodium restriction becomes more important although the use of newer and more effective medications has diminished the need for severe sodium restriction in many patients. We have recently completed a double-blind, placebo-controlled clinical trial

(a) *Despite being trim, this dog has good muscle tone with no evidence of muscle wasting (Cachexia score = 0).*

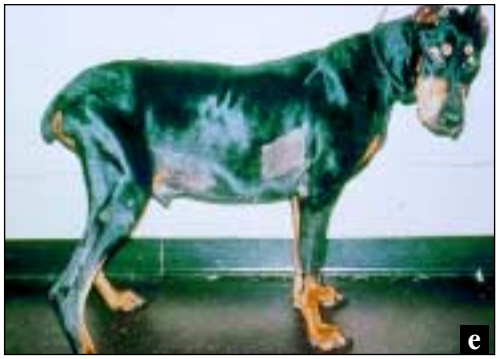
(b) *Early, mild muscle wasting is present in this dog, especially in the hindquarters and lumbar region (Cachexia score = 1).*



(c) *Moderate muscle wasting, apparent in all muscle groups, is present. Note especially the atrophy of the temporal muscles and muscles over the shoulder (Cachexia score = 2).*



(d) *Marked muscle wasting is present in this dog, as evidenced by the atrophy of all muscle groups (Cachexia score = 3).*



(e) *Severe muscle wasting can readily be seen in this dog (Cachexia score = 4).*

Figure 6 *A subjective cachexia score used by the author.*

Table 2

Recommendations for sodium restriction in dogs and cats with cardiac disease

1. Animals with cardiac disease without congestive heart failure:
   - Severe sodium restriction is not required
   - Counsel the owner to avoid diets high in sodium (sodium < 0.12 g/100 kcal) and to avoid treats or table food which are high in sodium
2. Early congestive heart failure:
   - Moderate sodium restriction (sodium < 0.09 g/100 kcal)
3. Severe congestive heart failure:
   - Moderate to severe sodium restriction (sodium < 0.04 g/100 kcal)

investigating the use of a sodium restricted diet in dogs with CHF. The results of this and future studies will help clinicians to better understand the pros and cons of sodium restriction and the most appropriate time to institute sodium restriction. Lacking this information, the author currently makes the recommendations for sodium restriction shown in **Table 2**. For an animal with cardiac disease without CHF (i.e. a dog with chronic valvular disease with no clinical signs or a asymptomatic cat with hypertrophic cardiomyopathy), the author counsels the owner to avoid diets high in sodium and to avoid treats or table food which are high in sodium. Most owners are unaware of the sodium content of pet foods and human foods and need very specific instructions regarding which foods are appropriate. Most will also appreciate recommendations for acceptable low salt treats (e.g. vegetables, fruits, low-salt commercial pet treats). When CHF first arises, additional sodium restriction is recommended. This does not necessarily require a therapeutic diet, but it is important to examine each individual diet to make sure it meets this restriction. Diets designed for animals with renal disease are not recommended for most cardiac patients because of the protein restriction, unless severe renal dysfunction is present. As CHF becomes more severe, more severe sodium chloride restriction may allow lower dosages of diuretics to be used to control clinical signs. To achieve severe sodium chloride restriction, it is usually necessary to feed a commercial therapeutic diet designed for cardiac patients. Typically, these diets are severely restricted in both sodium and chloride; levels of other nutrients vary with the individual product.

Potassium

Furosemide use has been implicated in the development of hypokalaemia due to increased urinary loss of potassium. Hypokalaemia can contribute to arrhythmias directly and by potentiating the arrhythmogenic effects of digitalis toxicosis. While hypokalaemia is relatively common in people using furosemide, it is uncommon in dogs and cats. In fact, the now common use of angiotensin converting enzyme (ACE) inhibitors decreases potassium excretion so can result in hyperkalaemia. Although clinically significant hyperkalaemia is uncommon, potassium supplementation or feeding diets with a high potassium content to animals receiving an ACE inhibitor may increase the risk for hyperkalaemia. Many commercial diets designed for animals with cardiac disease have increased concentrations of potassium so monitoring serum potassium concentrations for both elevated and depleted levels is important.

Magnesium

Like potassium, furosemide can cause hypomagnesaemia due to increased magnesium loss in the urine. Hypomagnesaemia can potentiate arrhythmias, decrease myocardial contractility and contribute to muscle weakness. Hypomagnesaemia, however, is not a consistent finding in canine studies, but this may be because serum magnesium concentrations are a very poor indicator of total body stores (18, 19). Nonetheless, if hypomagnesaemia is detected in an individual patient, especially in those patients with arrhythmias, supplementation should be instituted.

Vitamins

B vitamins

Thiamine deficiency is known to be a cause of cardiomyopathy in people, but there has been little investigation into the role of B vitamins as a cause of disease in dogs and cats. Recent research has shown that vitamin B_{12} is significantly lower in cats with cardiomyopathy than in healthy controls, an effect that appeared to be unrelated to diet (15). It is unclear whether this finding is cause or effect, but in rats, vitamin B_{12} deficiency has been shown to cause marked cardiac hypertrophy and myocardial fibrosis (20). Dogs and cats receiving furosemide have the potential for increased urinary loss of water soluble vitamins, although results of one study of cats with cardiomyopathy showed that cats receiving furosemide did not have lower concentrations of B vitamins than those not receiving furosemide (15). Human patients with CHF treated with furosemide, however, commonly have thiamine deficiency. Based on this information, B vitamin supplementation may be warranted in dogs and cats being treated with diuretics. Most commercial therapeutic diets designed for animals with cardiac disease contain increased levels of water soluble vitamins to offset urinary losses.

Other nutrients

Carnitine

L-Carnitine is concentrated in the skeletal and cardiac muscle and is critical for fatty acid metabolism and energy production. Carnitine deficiency is associated with primary myocardial disease in a number of species, including a family of Boxer dogs (21). Although anecdotal reports exist regarding the efficacy of carnitine in canine DCM, no blinded prospective studies have been done so a causative role has not been established. In fact, the myocardial carnitine deficiency seen in some dogs with DCM may be merely a secondary event. There are few side effects of carnitine supplementation but high cost is a deterrent for some owners. We currently offer the option of carnitine supplementation (50–100 mg/kg PO q 8 hours) to owners of dogs with DCM, but do not consider it obligatory. Research in human patients suggests that carnitine has no benefits in patients without carnitine deficiency.

Coenzyme Q10

Coenzyme Q10, like carnitine, is a co-factor in a number of reactions required for energy production and is also a potent antioxidant. Coenzyme Q10 has been proposed as a possible cause for DCM but this association has not been proven. Although most human studies have not been well controlled, some encouraging results have been found. Anecdotal reports of success in canine DCM have been made, but controlled, prospective studies will be necessary to accurately judge the efficacy of this product. The current recommended dosage is 30 mg PO BID, although up to 90 mg PO BID has been recommended for large dogs. It is unclear whether the benefits of supplementation are due to the correction of a deficiency or to pharmacological effects.

Antioxidants

A great deal of media attention has been given to antioxidants for their potential role in the prevention and treatment of human cardiac disease. Reactive oxygen species are a byproduct of oxygen metabolism for which the body normally compensates through the production of endogenous

antioxidants. An imbalance between oxidant production and antioxidant protection, however, may arise in certain situations. Although produced endogenously, antioxidants can also be supplied exogenously. The major antioxidants include enzymatic antioxidants (e.g. superoxide dismutase, catalase, glutathione peroxidase) and oxidant quenchers (e.g. vitamin C, vitamin E, glutathione and betacarotene). Most of the research in human cardiology has been done in coronary artery disease, but there is recent evidence that dogs with DCM have increased oxidative stress compared to normal dogs, and that vitamin E concentrations decrease as the disease progresses (22). Therefore, whilst much additional research is required, [*WALTHAM Focus* 2000; **10**(1) *WALTHAM Research News*] antioxidant supplementation may hold promise in the future for the therapy of dogs and cats with cardiac disease.

Conclusion

The increasing number of commercial diets available on the market has been a mixed blessing. While we now have a greater choice than ever before, it also can make the decision more difficult. Commercial therapeutic diets for dogs and cats with cardiac disease are available that are highly restricted in sodium. There also are other commercial diets that are moderately sodium-restricted that might be appropriate for early-to-moderate cardiac disease, but the levels of protein, fat, magnesium, potassium, fatty acids and other nutrients in these products vary, so careful selection is required. Selecting an optimal diet for each patient depends upon the stage of disease, clinical signs, laboratory parameters and appetite. Some diets may have the desired sodium level but are too low in protein for a cachectic patient, too high in fat for an obese patient or too high in potassium for a patient receiving an ACE inhibitor. Above all, the diet must be palatable enough that the animal will willingly eat it.

There is a great deal of potential for the use of nutritional supplementation in patients with cardiac disease, either to correct deficiencies or for their pharmacological effects. However, it is important to keep in mind that we need much additional information to define their role in the disease, when they should be used, when they should not be used, and optimal dosages. It is likely that, just as ideas on nutritional management have expanded and changed over the preceding decades, so too will they change in the upcoming years. It will be exciting to discover the new information that awaits us regarding nutritional modulation of cardiac disease in dogs and cats.

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